Docket No.: 12780/101

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT	:	Leonard et al.
SERIAL NO.	:	09/708,352
FILED	:	November 8, 2000
FOR	:	VACCINES FOR MYCOPLASMA BOVIS AND METHODS OF USE
EXAMINER:		Ford
GROUP ART UNIT	:	1645

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APPELLANTS' REPLY BRIEF

This Reply Brief is being filed to bring to the Board's attention a recent Federal Circuit decision that supports the Appellants' position and also because the Appellants believe that certain positions taken or statements made by the Examiner in the Examiner's Answer concerning the issues listed below merit a reply.

Limitations regarding protection against disease

The present claims contain limitations relating to protection against disease. For example, claim 1 requires that the claimed vaccine be "protective against *Mycoplasma bovis* clinical disease;" claim 29 recites "protective against *Mycoplasma bovis* mastitis."

The Examiner improperly refused to consider the effect on patentability of such limitations. According to the Examiner, such limitations are "intended uses" and thus cannot distinguish the present claims from the prior art. See, e.g., page 13 of the Examiner's Answer:

> In response to applicant's argument regarding that "the claimed vaccines are protective against *Mycoplasma bovis* mastitis", the Examiner is viewing this limitation as limitation of intended use. It should be remembered that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. [underscoring in original]

The Examiner's Answer repeats the above comments in the paragraph bridging pages 19 and 20.

The Appellants respectfully submit that the Examiner's position is erroneous. The Examiner's failure to consider the effect of the limitations relating to protection against disease on patentability is contrary to the recent decision by the Court of Appeals for the Federal Circuit in *In re Sullivan*, 498 F. 3d 1345, 84 U.S.P.Q. 2d 1034 (Fed. Cir. 2007), which issued after the filing date of the Appellants' Appeal Brief.

In Sullivan, the claim at issue was directed to a composition protective against snakebite that read as follows (italics in original):

> An antivenom *pharmaceutical* composition *for treating a snakebite victim,* comprising Fab fragments which bind specifically to a venom of a snake of the Crotalus genus and which are essentially free from contaminating Fc as determined by immunoelectrophoresis using anti-Fc antibodies, and a pharmaceutically acceptable carrier, *wherein said antivenom pharmaceutical composition neutralizes the lethality of the venom of a snake of the Crotalus genus.*

498 F. 3d at 1349, 84 U.S.P.Q. 2d at 1037.

The Appellant in *Sullivan* argued that the limitation requiring that the claimed composition "neutralizes the lethality of the venom" was not merely an intended use, but instead was a true claim limitation that should be considered in determining patentability

over the prior art. Furthermore, the Appellants argued that this limitation was a functional property that was unexpected in view of the prior art. The Appellant submitted expert declarations in support of their arguments.

The Board of Patent Appeal & Interferences refused to consider the expert declarations, viewing the claim language "*wherein said antivenom pharmaceutical composition neutralizes the lethality of the venom of a snake of the Crotalus genus*" as merely an intended use, and thus not relevant to patentability.

The Federal Circuit held that this was error.

> Furthermore, the Board's focus on the intended use of the claimed composition misses the mark. ... In this case, applicant does not concede that the only distinguishing factor of its composition is the statement of intended use and, in fact, extensively argues that its claimed composition exhibits the unexpected property of neutralizing the lethality of rattlesnake venom while reducing the occurrence of adverse immune reactions in humans. Such a use and unexpected property cannot be ignored. *See In re Papesch,* 50 C.C.P.A. 1084, 315 F.2d 381, 391 (1963) ("From the standpoint of patent law, a compound and all of its properties are inseparable; they are one and the same thing ... There is no basis in law for ignoring any property in making such a comparison."). The issue here is not whether a claim recites a new use, but whether the subject matter of the claim possesses an unexpected use. That unexpected property is relevant ...

498 F. 3d at 1353, 84 U.S.P.Q. 2d at 1040.

The language erroneously dismissed as an intended use not relevant to patentability by the Board in *Sullivan* has precisely the same import as the language dismissed by the Examiner in the present appeal. In both cases, the language at issue defines the claimed composition in terms of functional properties relating to providing a medical benefit. In both cases, the recited property is not shared by the prior art and would have been unexpected in view of the prior art.[1] According to *Sullivan* and *Papesch* (cited in *Sullivan*), such functional properties are inseparable from the composition itself and cannot be ignored.

Giving proper consideration to the functional properties recited in the present claims addresses the Examiner's concern in the above quoted passage from page 13 of the Examiner's Answer that there must be "a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art." [underscoring in original] If there are functional differences between the presently claimed vaccines and the prior art, there must be structural differences that give rise to those functional differences. Since the evidence of record (discussed in the Appeal Brief and herein below) shows that there are such functional differences between the presently claimed vaccines and the prior art, the evidence of record shows that there are structural differences between the presently claimed vaccines and the prior art.

Similarly, the lack of adverse reactions from the Appellants' vaccine is a functional property of the Appellants' vaccine that must result from some underlying

structural difference between the Appellants' vaccine and the prior art. Thus, the Examiner's failure to consider this functional property of the Appellants' vaccines was error. See page 13, second paragraph, of the Examiner's Answer.

The effectiveness of the vaccination in Boothby II

On page 20 of the Examiner's Answer, the Examiner referred to Boothby et al., 1986, Can. J. Vet. Res. 50:200-204 (Boothby II) and stated that Boothby II disclosed positive results for an *M. bovis* vaccine:

> With respect to Boothby, 1986, it should be noted that this study includes vaccinated cows without challenge and vaccinated cow [sic] with challenge, it should be noted that by the end of the study, no *M. bovis* could be recovered from challenged quarters on vaccinated cows and the milk production appeared mostly normal (Boothby 1986, Abstract). This is a positive assessment for the vaccinated cows. Thus, it cannot be concluded from these results that the vaccine did not work. In fact, it appears to prove the opposite

The Appellants submit that the Examiner is incorrect and has made a critical misinterpretation of the import of Boothby II. Rather than indicating success for the vaccine disclosed therein, Boothby II indicates complete failure for that vaccine. Indeed,

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[1] In the present appeal, evidence that the recited functional property is not shared by the prior art and thus was unexpected is found in Boothby II, Heller, and the Hanson publications, each of which is discussed below.

Boothby II reports that vaccination failed to prevent a drop in milk production, failed to prevent the infection of vaccinated udders, and resulted in an inflammatory response.

- Milk production

Figure 2, the lower portion of which shows milk production from challenged (deliberately infected with *M. bovis*) quarters (udders) of vaccinated (▲) and unvaccinated (●) cows, demonstrates that vaccination not only failed to improve milk production compared to non-vaccination, but actually resulted in poorer milk production. Figure 2 shows that both vaccinated and unvaccinated cows showed a steep decline in milk production until a time between weeks 13 and 14. Thereafter, milk production in the vaccinated cows remained at about its lowest level while milk production in unvaccinated cows improved to about 50% of the pre-challenge level.

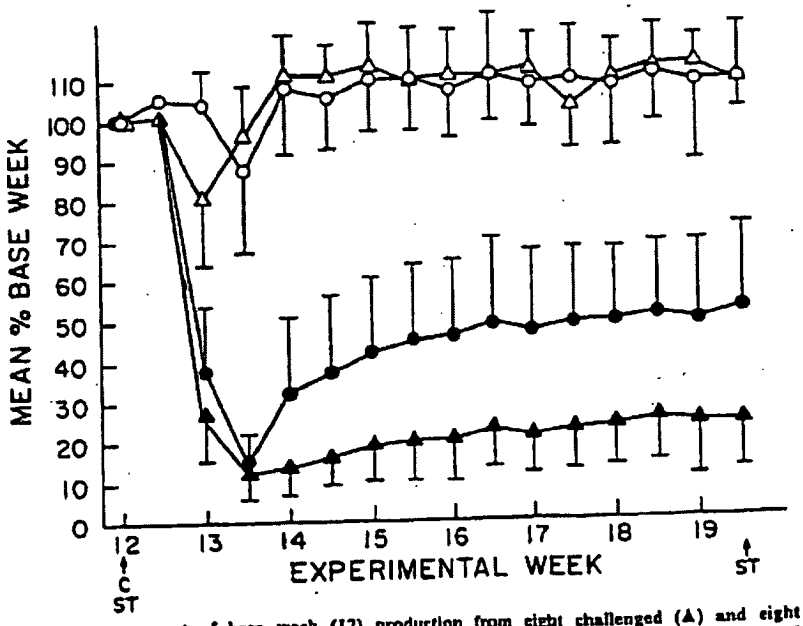

Fig. 2. Mean percent of base week (12) production from eight challenged (▲) and eight unchallenged (△) quarters on four vaccinated cows and eight challenged (●) and eight unchallenged (○) quarters on four control cows experimentally challenge exposed by intramammary infusion with live *M. bovis* and monitored for 7.5 weeks (weeks 12-19.5). (C = challenge exposure, ST = skin test).

Thus, Figure 2 indicates that vaccinated cows performed worse in terms of milk production than unvaccinated cows. Since Boothby II stated that a vaccine must have minimal effect on the productive capabilities of a cow in order to be considered efficacious[2], the vaccination here must be viewed as inefficacious, i.e., a failure.

- Lack of prevention of infection

Boothby II's vaccination was unable to prevent the infection of any quarters in vaccinated cows that were subsequently challenged with *M. bovis*. See page 202, middle column: "All experimentally challenged quarters became infected ..."

- Inflammation

More inflammation was observed in vaccinated than in unvaccinated cows. See page 203, right column: "The inflammation response occurred sooner and was more marked in vaccinates than in controls."

The passages referred to by the Examiner in the abstract of Boothby II pertain to observations made at the end of the study. Thus, given the abundant evidence discussed above that vaccination was ineffective or worse than no vaccination, the passages referred to by the Examiner appear to indicate no more than that, with the passage of sufficient time, the infections in the vaccinated cows resolved themselves spontaneously. This explanation is especially plausible when one considers that Boothby II reported that all challenged quarters on vaccinated cows remained positive for the California Mastitis

[2] See page 200, right column: "If prophylactic vaccination is to be efficacious, it must have minimal effects on the health and productive capabilities of the cow." See also page 203, middle column: "Systematic descriptions of milk production and milk quality during *M. bovis* infection, were important parameters in evaluating vaccine efficacy."

Test (CMT) throughout the study even though some quarters on non-vaccinated cows became negative. See page 202, right column: "All challenged quarters on vaccinated cows remained CMT-positive for the duration of the study while some challenged quarters on control cows because CMT-negative." Here again, worse results were seen for the vaccinated cows.

In view of the above, the Appellants must respectfully disagree with the Examiner's conclusion that Boothby II discloses a successful vaccine. Boothby II's vaccine was an abject failure.

Boothby II shows failure of others in the art to achieve the presently claimed invention. Boothby II would have discouraged those of ordinary skill in the art from following the path taken by the present inventors and thus represents a strong teaching away from the presently claimed invention.[3] Boothby II is therefore significant evidence that the rejection for obviousness under 35 U.S.C. §103(a) should be withdrawn.

The significance of the Heller and Hanson publications

On page 20 of the Examiner's Answer, the Examiner referred to Heller et al., 1993, Vet. Microbiol. 37:127-133 (Heller) and characterized Heller as follows:

> In response to Appellant's argument regarding Heller et al, 1993, it should be noted that Heller et al is directed to antigen capture of ELISA using a

[3] "A prior art reference may be considered to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be

monoclonal antibody for the detection of *Mycoplasma bovis* in milk. This reference does not teach or disclose a vaccine comprising an inactivated or attenuated *M. bovis* biotype, an adjuvant and an pharmaceutically acceptable excipient. Heller merely states that the spread of mastitis can be controlled by early detection.

The Examiner apparently views the above characterization of Heller as refuting the Appellants' position. Quite the opposite. Such a characterization either supports the Appellants' position or is not relevant to the present appeal.

That Heller "does not teach or disclose a vaccine comprising an inactivated or attenuated *M. bovis* biotype ..." supports the Appellants' position that the present claims are neither anticipated nor obvious. That Heller disclose an ELISA assay for the detection of *Mycoplasma bovis* in milk is irrelevant since the present claims are not directed to the detection of *M. bovis*.

Heller's teaching that the spread of mastitis should be controlled by early detection, without mention of vaccination, supports the Appellants' position that the art, including Boothby I (upon which the present anticipation rejection is based), had not achieved an inactivated or attenuated *M. bovis* preparation that was protective against *M. bovis* clinical disease. Otherwise, Heller would have mentioned vaccination as a way to control the spread of mastitis, not merely early detection. Heller therefore supports the Appellants' position that Boothby I does not anticipate the present claims.

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led in a direction divergent from the path that was taken by the applicant." *Monarch Knitting Mach. Corp. v. Sulzer Morat GmbH*, 139 F. 3d 877, 885, 45 U.S.P.Q. 2d 1977, 1984 (Fed. Cir. 1998).

On page 20 of the Examiner's Answer, the Examiner made statements about Hanson, (September, 2001) Bovine Veterinarian 4-8 and Hanson, (October, 2001) Bovine Veterinarian 12-20 (the Hanson publications) similar to those quoted above about Heller.

> In response to Appellant's argument regarding Hanson, September 2001 and October 2001, it should be noted that these references point out that *Mycoplasma* mastitis is a major problem in dairy industry. These references do not teach or disclose a vaccine comprising an inactivated or attenuated *M. bovis* biotype, an adjuvant and an [sic] pharmaceutically acceptable excipient. Contrary to Appellant's statements on the record, Heller et al, 1993, Hanson, September 2001 and Hanson, October 2001 were consider [sic] for their content and as they relate to *Mycoplasma bovis* problems associated with the dairy industry. However, as stated above, these references do not teach the claimed vaccine. They give an assessment of the problems mastitis has caused in the dairy industry and outline efforts to detect *Mycoplasma bovis* in milk samples.

The Appellants agree that the Hanson publications "do not teach or disclose a vaccine comprising an inactivated or attenuated *M. bovis* biotype ..." and "do not teach the claimed vaccine." That is why the Appellants made these publications of record. Like Heller, they demonstrate that, despite Boothby I, the art did not believe that a vaccine protective against *M. bovis* disease existed.

For the reasons stated in Appellants' opening Appeal Brief and in this Reply Brief, Appellants respectfully request that this appeal be granted and that the rejections of Appellants' claims be reversed, and that the claims at issue be found patentable.

Respectfully submitted,

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